STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 157375

TO: David Lukton
Location: REM/3B75/3C70
Art Unit: ~~1653~~ 1654 3C18
July 1, 2005

Case Serial Number: 09/869925

From: P. Sheppard
Location: Remsen Building
Phone: (571) 272-2529

sheppard@uspto.gov

Search Notes

ACCESS DB # _____

PLEASE PRINT CLEARLY

SEARCH REQUEST FORM
(STIC)

Requestor's Name: David Lukton Examiner number: 71263 Date: 6/23/05

Art Unit: 1653 Phone number: 571-272-0952 Serial Number: 09-869925

Mail Box: 3-C-70 Examiner Rm: 3-B-75 Results format: paper

* * * * * * * * * * * * *

Applicants are claiming the compounds on the attached sheet.

R^1, R^2 and R^3 = anything, with the proviso that at least two of R^1, R^2 and R^3 are alkyl;

R^4 = anything;

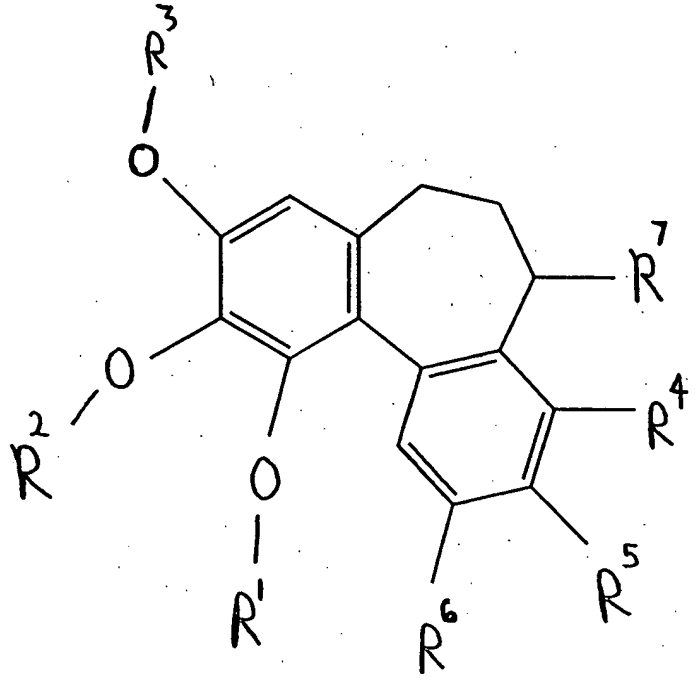
R^5 and R^6 can be anything, provided that both of the following conditions are met:

(a) R^5 or R^6 **is** -Y-R^{35},
wherein Y is one of the following: -C=O-, -OC=O-, -O-, -SO-, -SO_2-, -OSO_2-, -NH-, NH-C=O, -C=O-NH;

and wherein R^{35} is alkyl or alkoxy or alkanoyl or amino or alkylamino, or phenyl or benzyl, or R^{35} is an amino acid or a peptide;

(b) R^5 is **not** any of the following: hydroxyl, alkoxy, phosphate, acyl or benzyloxy

R^7 = hydrogen or hydroxyl or alkoxy or -N(R^8)R^9, wherein R^8 and R^9 can be anything


R3
O
R7
O
R4
R2
O
R1
R6
R5

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FILE 'HCAPLUS' ENTERED AT 17:03:59 ON 01 JUL 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 1 Jul 2005  VOL 143 ISS 2
FILE LAST UPDATED: 30 Jun 2005  (20050630/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=>
=>

=> d stat que
L3                STR
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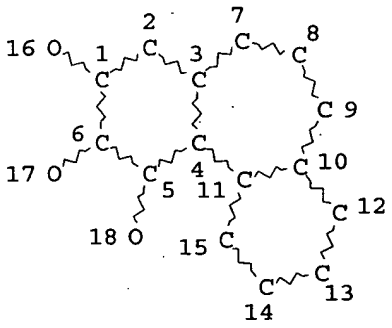


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DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  18

STEREO ATTRIBUTES: NONE
L5          667 SEA FILE=REGISTRY SSS FUL L3
L6              STR
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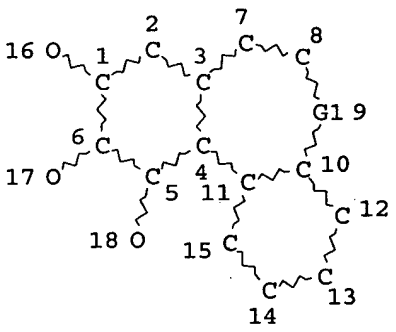

CH~G2 @19 20

O~Ak @21 22

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VAR G2=OH/21/N
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STEREO ATTRIBUTES: NONE
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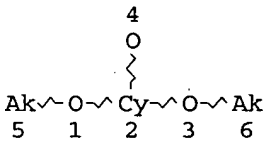

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DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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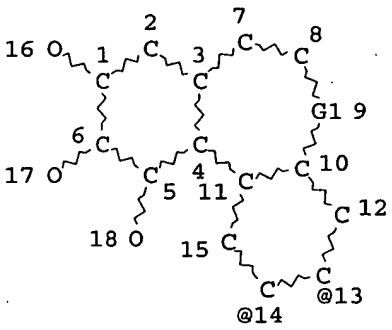

CH~G2 @19 20 O~Ak @21 22 G3~G4 23 24

C=O @26 27 O~C=O @28 @29 30 N~C=O @31 @32 33 O~SO2 @34 @35

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VAR G2=OH/21/N
VAR G3=14/13
VAR G4=26/28/29/O/S/N/31/32/34/35
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DEFAULT MLEVEL IS ATOM
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STEREO ATTRIBUTES: NONE
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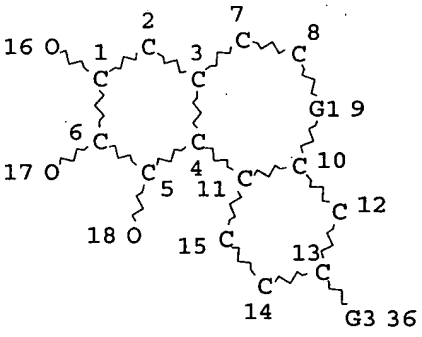

CH~G2 @19 20 O~Ak @21 22 O~Cb @37 38

VAR G1=CH2/19
VAR G2=OH/21/N
VAR G3=OH/21/P/37
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE
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L17         148 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16
L18          94 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND PD=<DECEMBER 24, 1999

L19           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 AND PATENT/DT


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=>

=> d ibib abs hitstr l19 1-7

L19  ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         1999:64693  HCAPLUS
DOCUMENT NUMBER:          130:125254
TITLE:                    Preparation and formulation of colchinol derivs.
                          useful for treatment of diseases involving
                          angiogenesis
INVENTOR(S):              Dougherty, Graeme
PATENT ASSIGNEE(S):       Angiogene Pharmaceuticals Ltd., UK
SOURCE:                   PCT Int. Appl., 30 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 9902166            A1    19990121    WO 1998-GB1977          19980706 <--
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, ML, MR, NE, SN, TD, TG
     CA 2292549            AA    19990121    CA 1998-2292549         19980706 <--
     AU 9882311            A1    19990208    AU 1998-82311           19980706 <--
     AU 741213             B2    20011129
     EP 1001785            A1    20000524    EP 1998-932374          19980706
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     BR 9810681            A     20000815    BR 1998-10681           19980706
     TR 9903149            T2    20000921    TR 1999-9903149         19980706
     NZ 501341             A     20010831    NZ 1998-501341          19980706
     JP 2001515516         T2    20010918    JP 1999-508313          19980706
     JP 3455549            B2    20031014
     RU 2232021            C2    20040710    RU 2000-102889          19980706
     ZA 9900106            A     19990707    ZA 1999-106             19990107 <--
     MX 9911154            A     20000930    MX 1999-11154           19991202
     US 6423753            B1    20020723    US 2000-477805          20000105
     NO 2000000077         A     20000107    NO 2000-77              20000107
PRIORITY APPLN. INFO.:                        GB 1997-14249       A   19970708
                                              WO 1998-GB1977      W   19980706
OTHER SOURCE(S):          MARPAT 130:125254
GI
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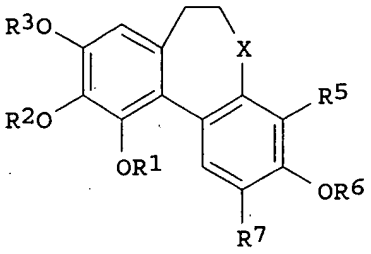

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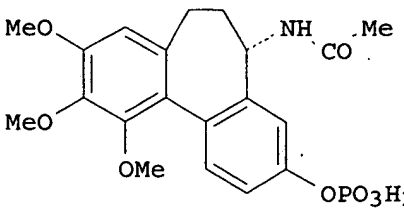


II

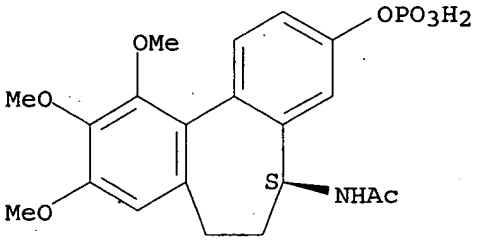
AB Colchinol derivs. I [R1, R2, R3, R6 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, alkanoyl, PO3H2; R5, R7 = H, alkyl, halogen, hydroxy, alkoxy, nitro, amino; X = CO, CS, CH2, CHR4, NR8R9; R4 = OH, alkoxy; R8 = H, alkyl, cycloalkyl, alkanoyl, thioalkanoyl, aryl, heteroaryl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl or arylaminosulfonyl; R9 = H, alkyl, cycloalkyl] were prepared and formulated for treatment of diseases involving angiogenesis. Thus, phosphate II was prepared via sequential O-phosphorylation of N-acetylcolchinol with (Me3CO)2PNEt2, P oxidation with MCPBA, and deesterification with TFA. The prepared compds were tested for activity against turmor vasculature with the compds. having R6 = OPO3H2 as most preferred.

IT **219923-05-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and formulation of colchinol derivs. useful for treatment of diseases involving angiogenesis)

RN 219923-05-4 HCAPLUS

CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

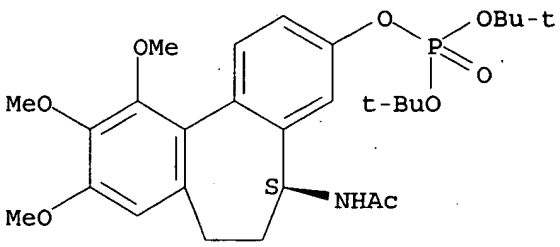


IT **219923-15-6P 219923-16-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and formulation of colchinol derivs. useful for treatment of diseases involving angiogenesis)

RN 219923-15-6 HCAPLUS

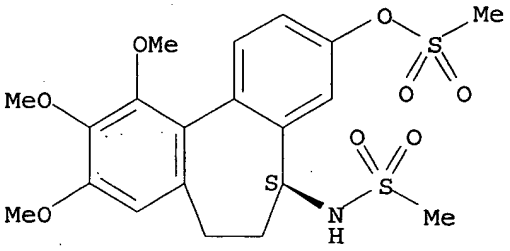
CN Phosphoric acid, (5S)-5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-3-yl bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 219923-16-7 HCAPLUS
CN Methanesulfonamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-[(methylsulfonyl)oxy]-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

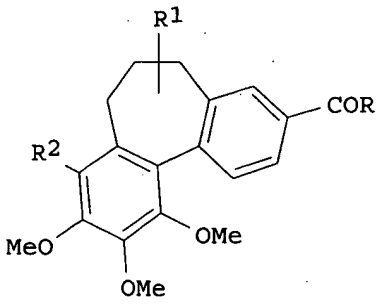


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:372619 HCAPLUS
DOCUMENT NUMBER: 129:36440
TITLE: Allocolchinones and uses thereof
INVENTOR(S): Timasheff, Serge M.; Gorbunoff, Marina J.; Perez-Ramirez, Bernardo
PATENT ASSIGNEE(S): Brandeis University, USA
SOURCE: U.S., 20 pp., Cont.-in-part of U. S. 527,372, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5760092	A	19980602	US 1996-615526	19960311 <--
PRIORITY APPLN. INFO.:			US 1995-527372 B2	19950913

OTHER SOURCE(S): MARPAT 129:36440
GI



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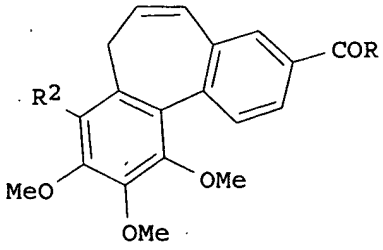

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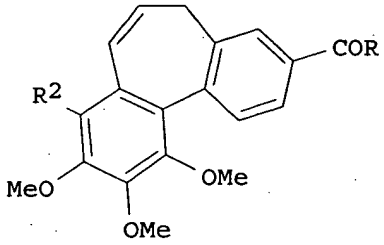


III

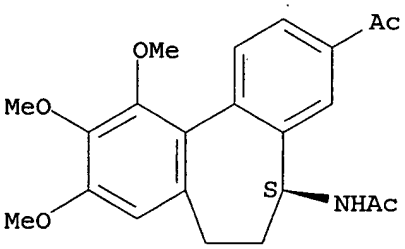
AB Disclosed are allocolchinones I, II, and III (R = Me, Et, and fluoromethyl, fluoroethyl; R1 = H, = O, amino, OH, SH, acyloxy, acylamino; R2 = H, alkoxy, cyano alkyl acylamino, alkoxycarbonyl, etc.), which are anti-mitotic agents. Allocolchinones bind to tubulin reversibly and are more effective at inhibiting microtubule formation than colchicine. 7-Acetamido-allocolchinone inhibits the growth of a number of tumor cell lines at concns. about 100 times lower than colchicine. Also disclosed is a method of treating an individual with cancer by administering a composition which comprises a therapeutically effective amount of an allocolchinone which inhibits microtubule assembly. Administering a therapeutically effective amount of a composition which comprises an allocolchinone which inhibits microtubule assembly can also be used for treating inflammatory diseases, multiple sclerosis, primary biliary cirrhosis, Alzheimer's disease and Behcet's disease.

IT **203984-10-5P 203984-11-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(antitumor activity of allocolchinones)

RN 203984-10-5 HCAPLUS

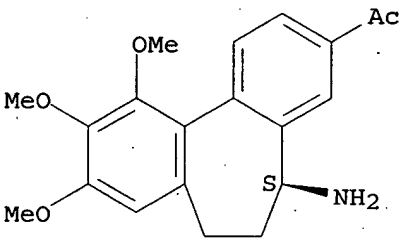
CN Acetamide, N-[(5S)-3-acetyl-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



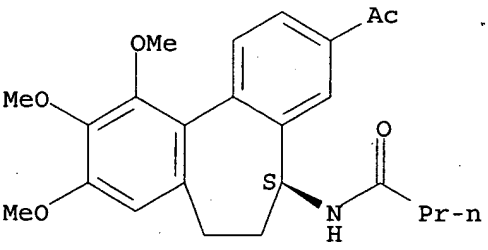
RN 203984-11-6 HCAPLUS
CN Ethanone, 1-[(5S)-5-amino-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cycloheptен-3-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



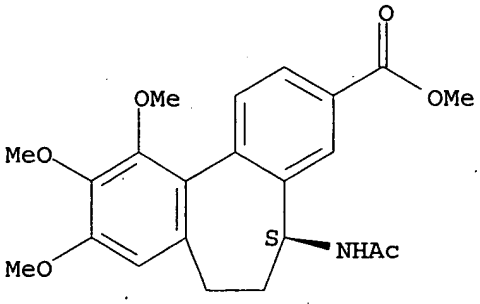
IT **203984-12-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor activity of allocolchinones)
RN 203984-12-7 HCAPLUS
CN Butanamide, N-[(5S)-3-acetyl-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cycloheptен-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **641-28-1**, Allocolchicine
RL: RCT (Reactant); RACT (Reactant or reagent)
(antitumor activity of allocolchinones)
RN 641-28-1 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1968:496938 HCAPLUS
DOCUMENT NUMBER: 69:96938
TITLE: N-Methylcolchicic acid amide
PATENT ASSIGNEE(S): Roussel-UCLAF
SOURCE: Fr. M., 4 pp.
CODEN: FMXXAJ
DOCUMENT TYPE: **Patent**
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 4685		19670123	FR	19650701 <--

GI For diagram(s), see printed CA Issue.

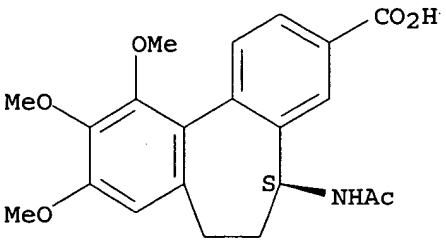
AB The title compound I was prepared from II. To a mixture of 400 cc. of CH2Cl2 and 24 cc. of HCONMe2 at 0° was added first 12 cc. POCl3 and then 20 g. of colchicine, the mixture stirred for 2 hrs. at 0° and poured into ice-water, and the organic layer washed with 0.1N NaOH and worked up to yield 84% II, m. 160° (CH2Cl2MeOH), [α]D -392° (c 0.35, CHCl3). II (5 g.) was added to a mixture of 25 cc. MeOH and 25 cc. aqueous 36% MeNH2, and the mixture stirred for 4.5 hrs. at room temperature to give 59% I, m. 225° and 238°, [α]D -140° (c 0.5, CHCl3). I has antiinflammatory properties. Pharmacol. test results are also given.

IT **6714-14-3DP**, Colchicic acid, derivs. **20395-99-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 6714-14-3 HCAPLUS

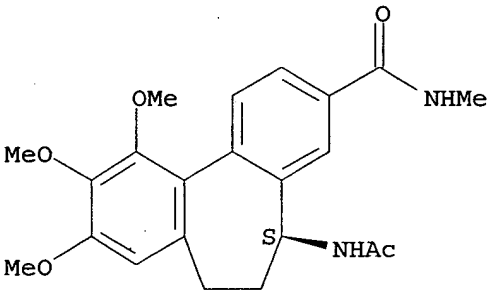
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 20395-99-7 HCAPLUS
CN Colchicamide, N9-methyl- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



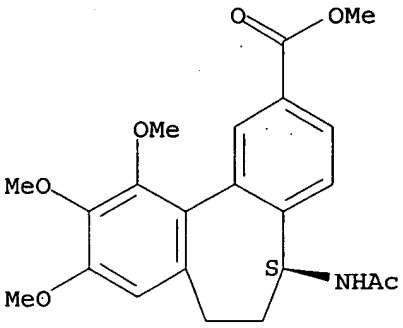
L19 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1963:415365 HCAPLUS
DOCUMENT NUMBER: 59:15365
ORIGINAL REFERENCE NO.: 59:2720h,2721a-b
TITLE: Dibenzocycloheptadiene carboxylic acid compounds
INVENTOR(S): Vaterlaus, Bruno P.; Muller, Georges; Velluz, Leon
PATENT ASSIGNEE(S): RousselUCLAF
SOURCE: 2 pp.
DOCUMENT TYPE: **Patent**
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2988568		19610613	US	<--
PRIORITY APPLN. INFO.:			FR	19570628

AB The title compds. (I), where R is H or Me, are useful for the modification of karyokinesis and the production of polyploids. In an example, 150 mg. of the sulfone of isothiocolchicine (V. and M., CA 50, 1733a) is dissolved in 1.5 cc. anhydrous MeOH containing 6 mg. Na. After refluxing, 1.5 h., the mixture is diluted with H2O and extracted with CHCl3. The separated aqueous layer is acidified and again extracted with CHCl3. Evaporation of the CHCl3 gives an oily product which is esterified with CH2N2 to yield the Me ester (I, R = Me) of 12, 13, 14-trimethoxy-3α-acetamido-4,5:6,7-dibenzocycloheptadiene-10-carboxylic acid, m. 177.5-8.5° (C6H6-Et2O-1:3), [α]20D -18° (0.5, CHCl8).
IT **613661-55-5**, 5H-Dibenzo[a,c]cycloheptene-2-carboxylic acid,

5α-acetamido-6,7-dihydro-9,10,11-trimethoxy-, methyl ester
(preparation of)
RN 613661-55-5 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-2-carboxylic acid, 5α-acetamido-6,7-dihydro-9,10,11-trimethoxy-, methyl ester (7CI) (CA INDEX NAME)

Absolute stereochemistry.

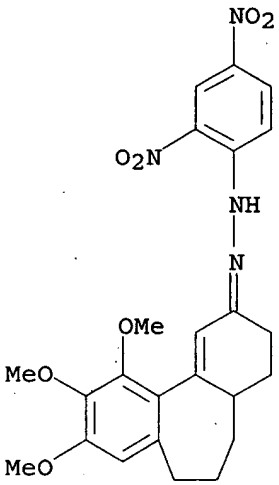


L19 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1962:429537 HCAPLUS
DOCUMENT NUMBER: 57:29537
ORIGINAL REFERENCE NO.: 57:5862f-h
TITLE: 2-Oxo - 2,3,4,4a,6,7 - hexahydro - 5H - dibenzo[a,c]cycloheptatrienes
INVENTOR(S): Kawazu, Kimishi Fujita Mitsutaka; Ayada, Kan
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd.
DOCUMENT TYPE: **Patent**
LANGUAGE: Unavailable
PATENT INFORMATION:

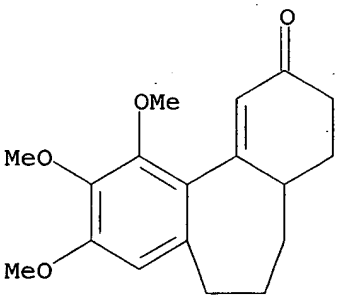
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 36017719		19610929	JP	19581227 <--

AB Methanolic solution (15 cc.) containing 3.2 g. 6-formyl-5-oxo-6,7,8,9-tetrahydro-5H-cycloheptabenzene, EtONa prepared from 0.39 g. Na and 15 cc. EtOH, and 15 cc. methanolic solution of ammonium salt (prepared from 5 g. 4-diethylamino-2-butanone and 5 g. MeI) are stirred in a N stream under ice cooling, poured into ice H2O, and the separated oil extracted with Et2O. The extract is evaporated, the residue dissolved in a mixture of 13 g. KOH, 34 cc. MeOH, and 30 cc. H2O, stirred in a N stream 4 hrs., then 1 l. saturated NaCl solution added, and extracted with Et2O to give 2.7 g. 2-oxo-2,3,4,4a,6,7-hexahydro-5H-dibenzo[a,c]cycloheptatriene, needles, m. 99-100°. Similarly are prepared 2-oxo-9,10-dimethoxy-2,3,4,4a,6,7-hexahydro-5H-dibenzo[a,c]cycloheptatriene, columns, m. 114-16° (2,4-dinitrophenylhydrazone m. 235-7°), and 2-oxo-9,10,11 - trimethoxy - 2,3,4,4a,6,7 - hexahydro-5H-dibenzo[a,c]cycloheptatriene, m. 103.5-5° (2,4-dinitrophenylhydrazone m. 181-2°). The compds. were useful intermediates for manufacture of colchinol methyl ether.
IT **103592-69-4**, 2H-Dibenzo[a,c]cyclohepten-2-one, 3,4,4a,5,6,7-hexahydro-9,10,11-trimethoxy-, (2,4-dinitrophenyl)hydrazone
131927-14-5, 2H-Dibenzo[a,c]cyclohepten-2-one, 3,4,4a,5,6,7-hexahydro-9,10,11-trimethoxy-
(preparation of)

RN 103592-69-4 HCAPLUS
CN 2H-Dibenzo[a,c]cyclohepten-2-one, 3,4,4a,5,6,7-hexahydro-9,10,11-trimethoxy-, (2,4-dinitrophenyl)hydrazone (6CI, 7CI) (CA INDEX NAME)



RN 131927-14-5 HCAPLUS
CN 2H-Dibenzo[a,c]cyclohepten-2-one, 3,4,4a,5,6,7-hexahydro-9,10,11-trimethoxy- (9CI) (CA INDEX NAME)



L19 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1961:64828 HCAPLUS
DOCUMENT NUMBER: 55:64828
ORIGINAL REFERENCE NO.: 55:12322a-b
TITLE: Substituted dibenzocycloheptadienes
PATENT ASSIGNEE(S): U C L A F
DOCUMENT TYPE: **Patent**
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 839164		19600629	GB	<--

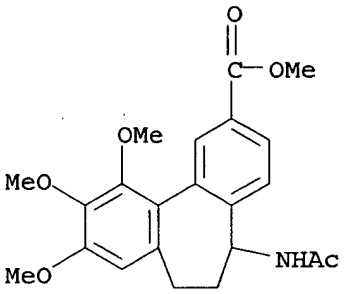
AB A solution of 150 mg. of the sulfone of isothiocolchicine in 1.5 ml. absolute MeOH containing 6 mg. Na is refluxed 1.5 hrs., diluted with H2O, and extracted with

CHCl3. The aqueous liquid is acidified and reextd. with CHCl3 to give 12,13,14-trimethoxy-3α-acetamido-4,5,6,7-dibenzocycloheptadiene-10-carboxylic acid (I). I is esterified with CH2N2 to give the Me ester, m. 177.5-8.5°, [α]20D -18° (c 0.5, CHCl3).

IT **105991-87-5**, 5H-Dibenzo[a,c]cycloheptene-2 carboxylic acid, 5-acetamido-6,7-dihydro-9,10,11-trimethoxy-, methyl ester
114034-82-1, 5H-Dibenzo[a,c]cycloheptene-2 carboxylic acid, 5-acetamido-6,7-dihydro-9,10,11-trimethoxy-
(preparation of)

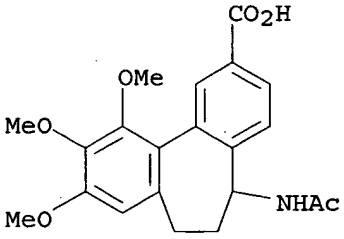
RN 105991-87-5 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-2-carboxylic acid, 5-acetamido-6,7-dihydro-9,10,11-trimethoxy-, methyl ester (6CI, 7CI) (CA INDEX NAME)



RN 114034-82-1 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-2-carboxylic acid, 5-acetamido-6,7-dihydro-9,10,11-trimethoxy- (6CI) (CA INDEX NAME)



L19 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1960:128763 HCAPLUS
DOCUMENT NUMBER:	54:128763
ORIGINAL REFERENCE NO.:	54:24616b-e
TITLE:	Derivatives of 12,13,14-trimethoxy-4,5:6,7-dibenzocycloheptadiene-8-carboxylic acid
INVENTOR(S):	Vaterlaus, Bruno; Furlenmeier, Andre
PATENT ASSIGNEE(S):	U C L A F
DOCUMENT TYPE:	**Patent**
LANGUAGE:	Unavailable
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 2944078		19600705	US		<--

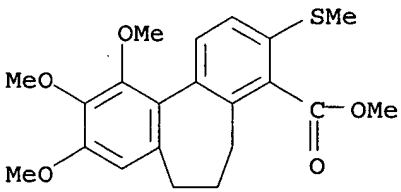
DE 1098519 DE

AB A solution of N-deacetylthiocolchicine (1 g.) in 75 ml. MeOH was stirred at room temperature for 24 hrs. with 10 ml. MeI and 0.5 g. Na2CO3 and filtered. The filtrate was evaporated to dryness and treated with Ac2O and pyridine to acetylate any monomethyl derivative formed as byproduct. The mixture was diluted with ice water and extracted with CHCl3. N-Deacetyl-N, N-dimethylthiocolchicine (I) was extracted from the CHCl3 by 6N H2SO4. The base was liberated by addition of alkali and extracted with CHCl3. Crystallization from EtOAc of the residue obtained by evaporation of CHCl3 left 633 mg. I, orange, m. 169-70° (decomposition), [α]D20 -150 ± 5° (0.5%, CHCl3); I.MeI, yellow, m. 201-3° (decomposition). I.MeI (1.0 g.) was treated with 2.5 g. freshly prepared Ag2O in 100 ml. MeOH and 8 ml. H2O. Me3N was evolved at once. The reaction was completed by 4 hrs. stirring at 40°. The solution was filtered and evaporated in vacuo. Crystallization of the residue from MeOH with C gave 275 mg. needles, m. 159-60°, [α]D20 0°, of Me 12,13,14-trimethoxy-9-methylthio-4,5:6,7-dibenzocycloheptadiene-8-carboxylate (II). Desulfurization of II was carried out by hydrogenating 100 mg. in 25 ml. EtOAc in the presence of 2.5 ml. Raney Ni suspension. The filtrate from the catalyst was evaporated The residue crystallized on trituration with Et2O to give 66 mg. needles of Me 12,13,14-trimethoxy-4,5:6,7-dibenzocycloheptadiene-8-carboxylate (III), m. 152°, [α]D20 0°. III (125 mg.) was saponified by refluxing in 50% EtOH-H2O and alkali. The acidified solution was extracted with CHCl3 to give after evaporation 75 mg. free acid, m. 184°, [α]D° 0°. The compds. are employed as 0.1-0.2% solns. in agriculture to produce polyploidism.

IT **115003-37-7**, 5H-Dibenzo[a,c]cycloheptene-4-carboxylic acid, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, methyl ester (preparation of)

RN 115003-37-7 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-4-carboxylic acid, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, methyl ester (6CI) (CA INDEX NAME)



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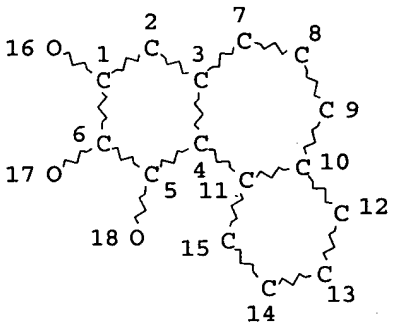

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
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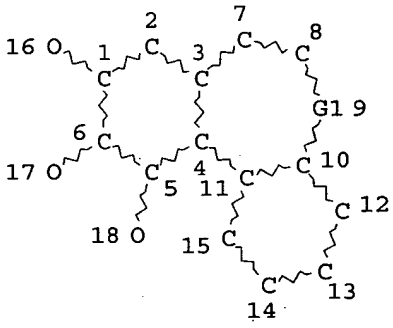

CH~G2 O~Ak
@19 20 @21 22

VAR G1=CH2/19
VAR G2=OH/21/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
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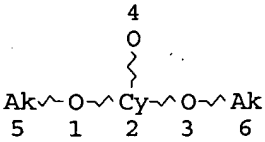

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 6

STEREO ATTRIBUTES: NONE
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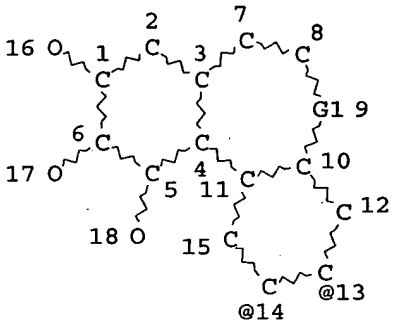
L11 STR



CH~G2 @19 20 O~Ak @21 22 G3~G4 23 24

C=O @26 27 O~C=O @28 @29 30 N~C=O @31 @32 33 O~SO2 @34 @35

VAR G1=CH2/19
VAR G2=OH/21/N
VAR G3=14/13
VAR G4=26/28/29/O/S/N/31/32/34/35
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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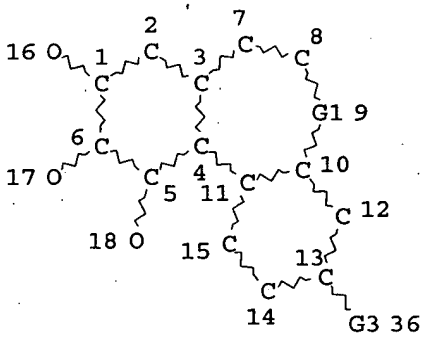

CH~G2 @19 20 O~Ak @21 22 O~Cb @37 38

VAR G1=CH2/19
VAR G2=OH/21/N
VAR G3=OH/21/P/37

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE
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L17 148 SEA FILE=HCAPLUS ABB=ON PLU=ON L16
L18 94 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND PD=<DECEMBER 24, 1999

L19 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 AND PATENT/DT
L24 87 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 NOT L19

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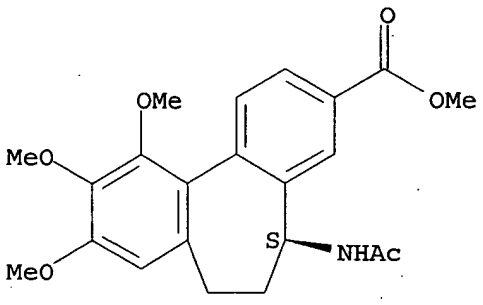
L24 ANSWER 1 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:532100 HCAPLUS
DOCUMENT NUMBER: 131:157851
TITLE: Axial configuration of optically active colchicinoids and allocolchicinoids. A correction
AUTHOR(S): Brossi, Arnold; Lee, Huo-Hsiung; Yeh, Herman J. C.
CORPORATE SOURCE: Natural Products Laboratory, Division Medicinal Chemistry Natural Products, School Pharmacy, Univ. North Carolina, Chapel Hill, NC, USA
SOURCE: Helvetica Chimica Acta (**1999**), 82(8), 1223-1224
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Correction of the axial configuration of (-)-rotating colchicinoids and allocolchicinoids from (aS) to (aR) is reported.
IT **641-28-1**, Allocolchicine
RL: MSC (Miscellaneous)
(axial configuration of colchicinoids and allocolchicinoids, correction)
RN 641-28-1 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS

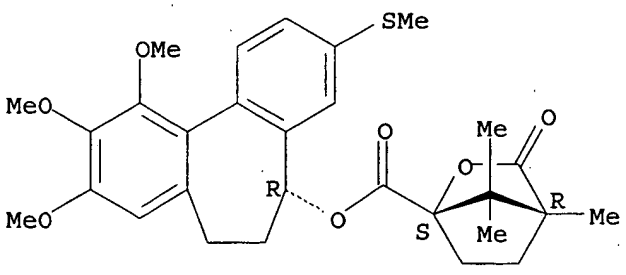
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:408101 HCAPLUS
DOCUMENT NUMBER: 129:81874
TITLE: Antitumor agents. Part 184. Syntheses and antitubulin activity of compounds derived from reaction of thiocolchicone with amines. Lactams, alcohols, and ester analogs of allothiocolchicinoids
AUTHOR(S): Shi, Qian; Chen, Ke; Brossi, Arnold; Verdier-Pinard, Pascal; Hamel, Ernest; McPhail, Andrew T.; Lee, Kuo-Hsiung
CORPORATE SOURCE: Natural Products Lab. Div. Med. Chem. Natural Products, School Pharmacy, Univ. North Carolina, Chapel Hill, NC, 27599, USA
SOURCE: Helvetica Chimica Acta (**1998**), 81(6), 1023-1037
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta AG
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:81874

AB 7-O-substituted analogs of deaminodeoxycolchinol thiomethyl ether were synthesized and evaluated for their inhibitory effects on tubulin polymerization in vitro. Unexpectedly, introduction of O-aroyl substituents at C(7) of the new compds. resulted in different effects on the conformation of the biphenyl backbone and, therefore, on biol. activity. The biol. active O-acyl derivs. retained the (-)-(aS,7S)-configuration of colchicine, but, among the O-aroyl derivs., the (+)-(7R)-isomers had greater inhibitory effects on tubulin than the (-)-(7S)-derivs. Anal. of 1H-NMR spectra and optical rotatory data indicated that, in solution, both (7S)- and (7R)-compds. assumed 2 conformations, and that biol. activity is related to the proportion of the (aS)-conformation.

IT **209467-07-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(crystal structure and antitubulin activity)
RN 209467-07-2 HCAPLUS
CN 2-Oxabicyclo[2.2.1]heptane-1-carboxylic acid, 4,7,7-trimethyl-3-oxo-, (5R)-6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cyclohepten-5-yl ester, (1S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

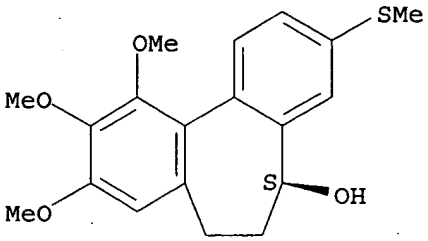


IT **209467-08-3P 209467-10-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); SPN

(Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitubulin activity of thiocolchicine analogs as antitumors)

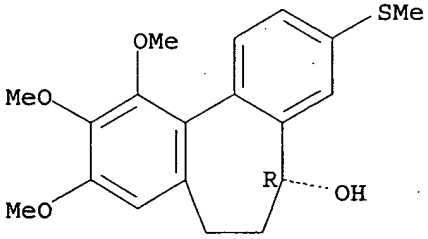
RN 209467-08-3 HCAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-ol, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



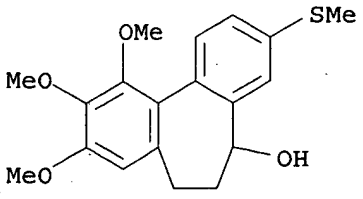
RN 209467-10-7 HCAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-ol, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **209466-99-9P 209467-06-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitubulin activity of thiocolchicine analogs as antitumors)

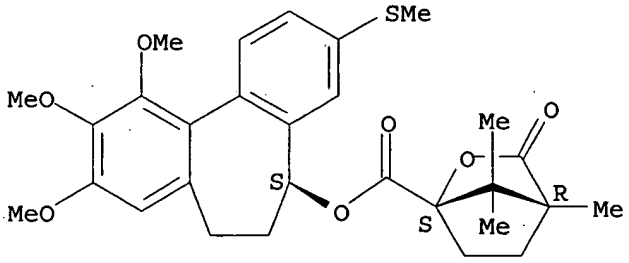
RN 209466-99-9 HCAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-ol, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)- (9CI) (CA INDEX NAME)



RN 209467-06-1 HCAPLUS
CN 2-Oxabicyclo[2.2.1]heptane-1-carboxylic acid, 4,7,7-trimethyl-3-oxo-,

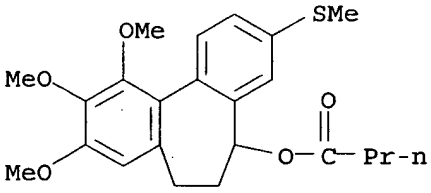
(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cyclohepten-5-yl ester, (1S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

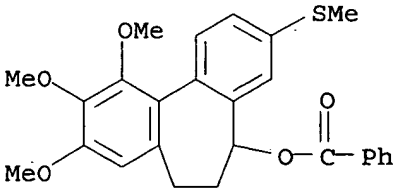


IT **209467-00-5P 209467-01-6P 209467-02-7P**
209467-03-8P 209467-04-9P 209467-05-0P
209467-11-8P 209467-12-9P 209467-13-0P
209467-14-1P 209467-15-2P 209467-16-3P
209467-17-4P 209467-18-5P 209467-19-6P
209467-20-9P 209467-21-0P 209467-22-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitubulin activity of thiocolchicine analogs as antitumors)

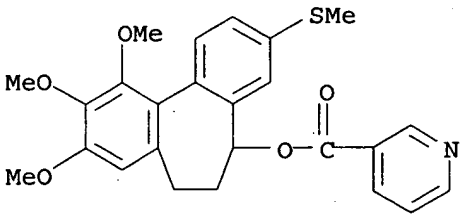
RN 209467-00-5 HCAPLUS
CN Butanoic acid, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cyclohepten-5-yl ester (9CI) (CA INDEX NAME)



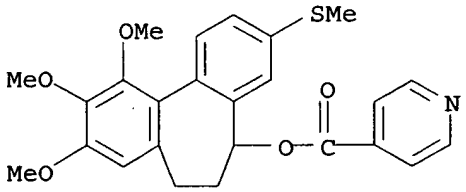
RN 209467-01-6 HCAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-ol, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, benzoate (9CI) (CA INDEX NAME)



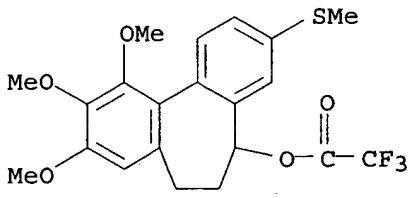
RN 209467-02-7 HCAPLUS
CN 3-Pyridinecarboxylic acid, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cyclohepten-5-yl ester (9CI) (CA INDEX NAME)



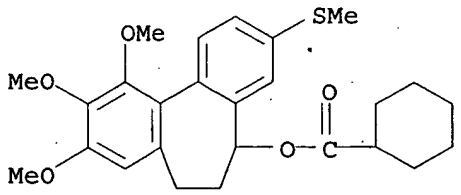
RN 209467-03-8 HCAPLUS
CN 4-Pyridinecarboxylic acid, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cyclohepten-5-yl ester (9CI) (CA INDEX NAME)



RN 209467-04-9 HCAPLUS
CN Acetic acid, trifluoro-, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cyclohepten-5-yl ester (9CI) (CA INDEX NAME)

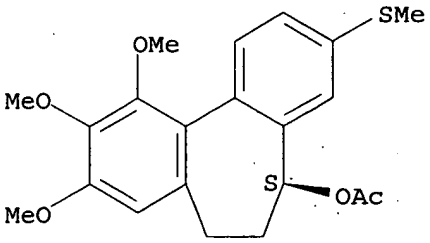


RN 209467-05-0 HCAPLUS
CN Cyclohexanecarboxylic acid, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cyclohepten-5-yl ester (9CI) (CA INDEX NAME)



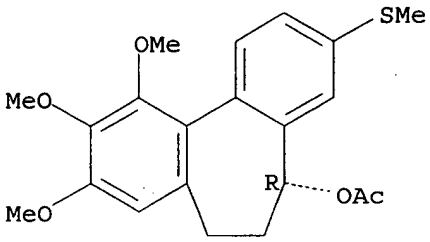
RN 209467-11-8 HCAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-ol, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, acetate, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



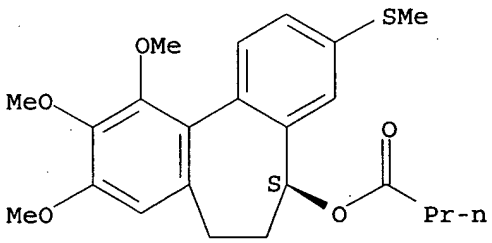
RN 209467-12-9 HCAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-ol, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, acetate, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



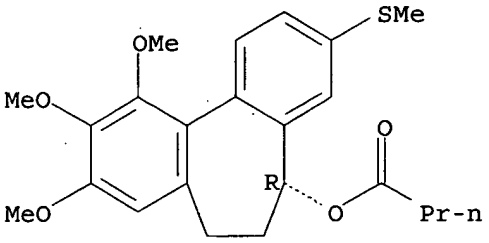
RN 209467-13-0 HCAPLUS
CN Butanoic acid, (5S)-6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cyclohepten-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



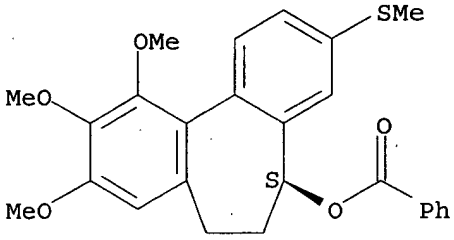
RN 209467-14-1 HCAPLUS
CN Butanoic acid, (5R)-6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cyclohepten-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



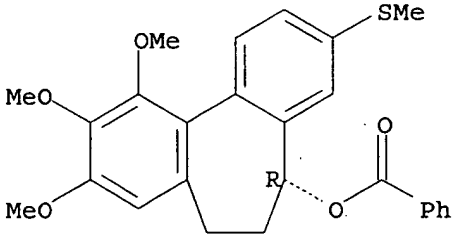
RN 209467-15-2 HCAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-ol, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, benzoate, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



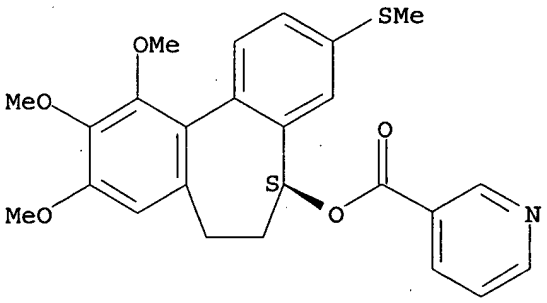
RN 209467-16-3 HCAPLUS
CN 5H-Dibenzo[a,c]cyclohepten-5-ol, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, benzoate, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



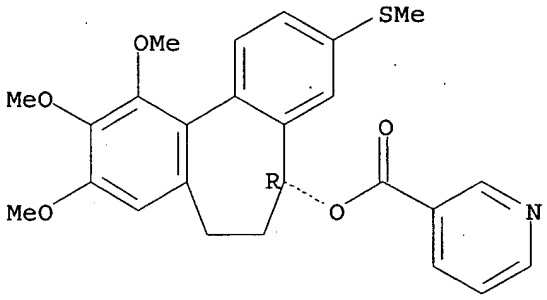
RN 209467-17-4 HCAPLUS
CN 3-Pyridinecarboxylic acid, (5S)-6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cyclohepten-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



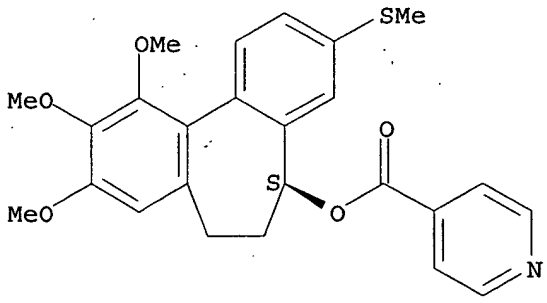
RN 209467-18-5 HCAPLUS
CN 3-Pyridinecarboxylic acid, (5R)-6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cycloheptен-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



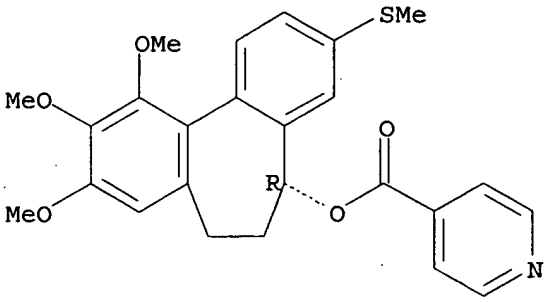
RN 209467-19-6 HCAPLUS
CN 4-Pyridinecarboxylic acid, (5S)-6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cycloheptен-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



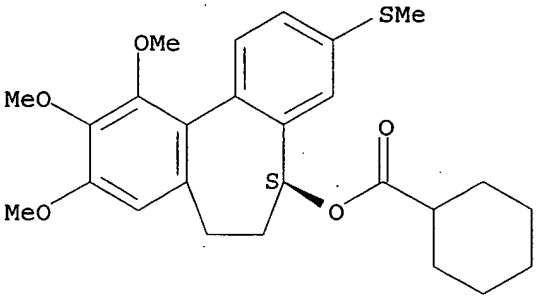
RN 209467-20-9 HCAPLUS
CN 4-Pyridinecarboxylic acid, (5R)-6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cycloheptен-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



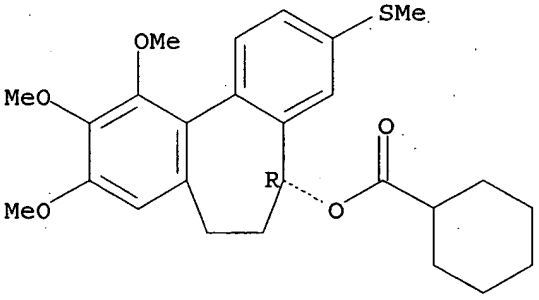
RN 209467-21-0 HCAPLUS
CN Cyclohexanecarboxylic acid, (5S)-6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cycloheptен-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 209467-22-1 HCAPLUS
CN Cyclohexanecarboxylic acid, (5R)-6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-5H-dibenzo[a,c]cycloheptен-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



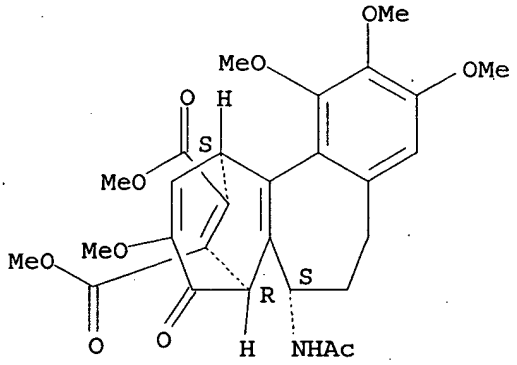
L24 ANSWER 10 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:303141 HCAPLUS
DOCUMENT NUMBER: 127:34391
TITLE: Positional and facial selectivity in Diels-Alder reactions of (-)-(aS,7S)-colchicine. Synthesis of novel analogs of the alkaloid
AUTHOR(S): Brecht, Rene; Haenel, Frank; Seitz, Gunther; Frenzen,

Gerlinde; Pilz, Astrid; Massa, Werner; Wocadlo, Sigrid
CORPORATE SOURCE: Pharmazeutisch-Chemisches Institut, Univ. Marburg, Marburg, D-35032, Germany
SOURCE: Liebigs Annalen/Recueil (**1997**), (5), 851-857
CODEN: LIARFV
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:34391
AB The positional and facial selectivity in Diels-Alder reactions of several hetero- and carbodienophiles with (-)-(aS,7S)-colchicine (I) was examined In all cases, cycloaddn. occurred with high positional selectivity at the 8,12-positions of the alkaloid and preferentially from the diene face syn to the allylic substituent at the stereogenic center C(7). The observed high π-facial diastereoselectivity is independent of the polarity of the solvent used and is therefore probably a consequence of steric factors. The structures of Diels-Alder adducts of I with singlet O, N-phenyl-1,2,4-triazolinedione and trans-cyclooctene were assigned on the basis of spectral data and verified by x-ray crystallog.

IT **190837-82-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(selectivity in Diels-Alder reactions of colchicine and preparation of analogs)

RN 190837-82-2 HCAPLUS
CN 8,12-Ethenobenzo[a]heptalene-13,14-dicarboxylic acid, 7-(acetylamino)-5,6,7,8,9,12-hexahydro-1,2,3,10-tetramethoxy-9-oxo-, dimethyl ester, (7S,8R,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L24 ANSWER 15 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:115633 HCAPLUS
DOCUMENT NUMBER: 124:138941
TITLE: Stoichiometric and substoichiometric inhibition of tubulin self-assembly by colchicine analogs
AUTHOR(S): Perez-Ramirez, Bernardo; Andreu, Jose M.; Gorbunoff, Marina J.; Timasheff, Serge N.
CORPORATE SOURCE: Graduate Department of Biochemistry, Brandeis University, Waltham, MA, 02254-9110, USA
SOURCE: Biochemistry (**1996**), 35(10), 3277-85
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

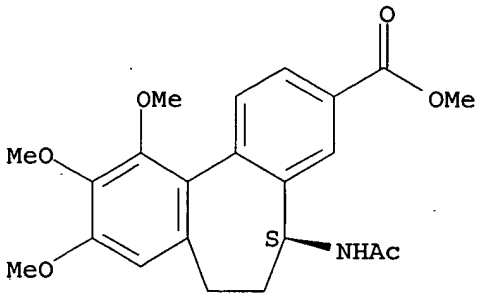
AB The mechanism of the stoichiometric and substoichiometric inhibitions of tubulin self-assembly by several structural analogs of colchicine (COL) was investigated. The inhibition data were analyzed in terms of a simple model that takes into consideration Kg, the normal microtubule growth constant, equal to Cr-1 (Cr is the critical concentration for microtubule formation), and Kb, the binding constant of the drug to tubulin. In this manner, the value of the microtubule inhibition constant (Ki), which is the binding constant of the tubulin-drug complex to the end of a growing microtubule (which stops the microtubule growth), was determined The results of the anal. of microtubule inhibition by the various colchicine analogs show that all the inhibitions can be expressed reasonably by this model. The strongest inhibitors found were colchicine (COL), allocolchicine (ALLO), and the biphenyl keto analog 2,3,4-trimethoxy-4'-acetyl-1,1'-biphenyl (TKB), which had essentially identical values of Ki = (2.1) + 106 M-1. MTC, the two-ring analog of colchicine, was weaker (Ki = 5.6+105 M-1). A most striking result was that tropolone Me ether (TME), which is ring C of COL, and which binds very weakly to tubulin (Kb = 3.5+102 M-1), is a substoichiometric inhibitor. Its Ki value of 8.7+105 M-1 makes it identical in strength to MTC, suggesting that ring A makes little or no contribution to the induction of assembly inhibition. The three biphenyls, which bind to tubulin with similar affinity, spanned the spectrum from strong substoichiometric inhibition (TKB) to stoichiometric inhibition for 2,3,4-trimethoxy-4'-carbomethoxy-1,1'-biphenyl (TCB) and an intermediate mode for the methoxy derivative 2,3,4,4'-tetramethoxy-1,1'-biphenyl (TMB). The extent of tubulin bound to drugs at 50% inhibition (r) was .apprx.2% for TKB, ALLO, and COL, i.e., one liganded tubulin for every 40-50 mols. of free protein (substoichiometric). This ratio was 1:1.5 for TCB (stoichiometric) and 1:6 for TMB (intermediate). For TME, which is a single ring compound, it was 1:25. The progression of the stoichiometries varied directly with Ki and was totally unrelated to the values of Kb, which indicated the control of the stoichiometry by Ki and the close thermodn. linkage between r and Ki. Comparison of the inhibitory capabilities of the various drugs identified the need for strong substoichiometric inhibition of a carbonyl group on ring C or C'. Furthermore, this group must be properly oriented by interaction with the protein or by the structural rigidity imparted by ring B, as in ALLO. The simple linked equilibrium model developed in this paper permits the alignment of drugs along a continuum that ranges from stoichiometric to strong substoichiometric modes of microtubule inhibition. Furthermore, it shows that the previously identified two classes are the two ends of a monotonously progressing spectrum described by a single mechanism of action.

IT **641-28-1**, Allocolchicine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(stoichiometric and substoichiometric inhibition of tubulin self-assembly by colchicine analogs)

RN 641-28-1 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



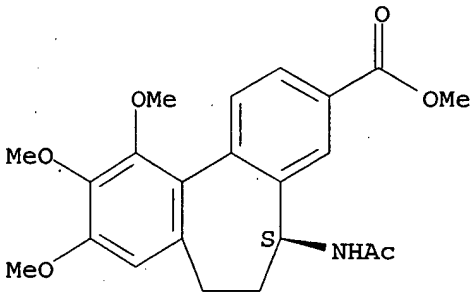
L24 ANSWER 20 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:598774 HCAPLUS
DOCUMENT NUMBER: 121:198774
TITLE: Energy Transfer Studies of the Distances between the Colchicine, Ruthenium red, and BisANS Binding Sites on Calf Brain Tubulin
AUTHOR(S): Ward, Larry D.; Seckler, Robert; Timasheff, Serge N.
CORPORATE SOURCE: Graduate Department of Biochemistry, Brandeis University, Waltham, MA, 02254-9110, USA
SOURCE: Biochemistry (**1994**), 33(39), 11900-8
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fluorescence energy transfer expts. were performed in order to measure the spatial separation between the colchicine and Ruthenium red binding sites, the high-affinity bisANS and Ruthenium red sites, and the allocolchicine and high-affinity bisANS sites on calf brain tubulin. Energy transfer was observed between both colchicine and allocolchicine and Ruthenium red, resulting in a distance of 40-45 Å between these sites on the tubulin mol. No detectable energy transfer could be observed when allocolchicine was used as fluorescence donor and bisANS as acceptor or when bisANS was used as donor and Ruthenium red as acceptor. This indicates that the distance of separation between the allocolchicine and bisANS sites is greater than 50 Å, while that between the bisANS and Ruthenium red sites is greater than 72 Å. On the basis of these and previous distance measurements (Ward & Timasheff, 1988), two triangles of binding sites have been defined (colchicine-bisANS-E-site and colchicine-bisANS-Ruthenium red). Since the dihedral angle between them is not known, a schematic model has been drawn with all the sites located in a single plane. Incorporation of the recently identified location of the colchicine site on the β-subunit (Shearwin & Timasheff,1994), the assignment of the exchangeable GTP binding site to the N-terminal region of the β-subunit distant from the αβ interface (Kirchner & Mandelkow, 1985), and the proposed chemical environments of the various sites result in a model in which the Ruthenium red binding site is on the α-subunit closest to the strongly anionic C-terminal region, the colchicine site is on the β-subunit with ring A oriented toward the αβ intersubunit interface, the nucleotide E-site is in the N-terminal domain of the same subunit in the region of formation of the longitudinal bond in protofilament assembly, and the high-affinity bisANS (or ANS) site is in a hydrophobic region of the same domain.

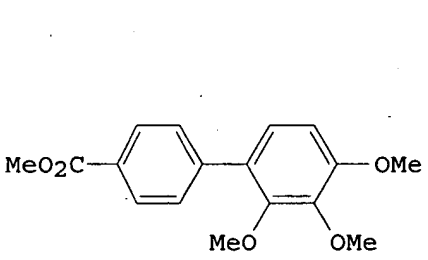
IT **641-28-1**, Allocolchicine
RL: BIOL (Biological study)
(tubulin αβ dimer binding by, structural characterization of site for)

RN 641-28-1 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 25 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:191308 HCAPLUS
DOCUMENT NUMBER: 118:191308
TITLE: Synthesis and tubulin-binding properties of some AC- and ABC-ring analogs of allocolchicine
AUTHOR(S): Banwell, Martin G.; Cameron, Jennifer M.; Corbett, Madeline; Dupuche, Joseph R.; Hamel, Ernest; Lambert, John N.; Lin, Chii M.; Mackay, Maureen F.
CORPORATE SOURCE: Sch. Chem., Univ. Melbourne, Parkville, 3052, Australia
SOURCE: Australian Journal of Chemistry (**1992**), 45(12), 1967-82
CODEN: AJCHAS; ISSN: 0004-9425
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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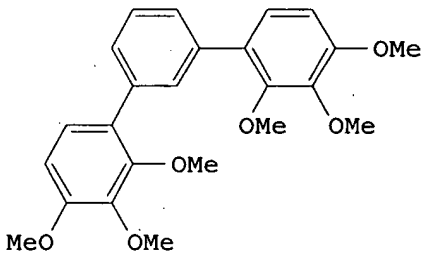
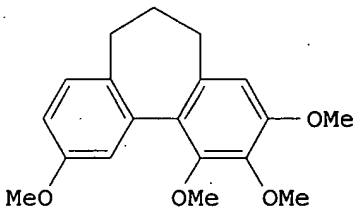


II



III

AB Fourteen title compds., e.g. the Me (trimethoxyphenyl)benzoate I, the

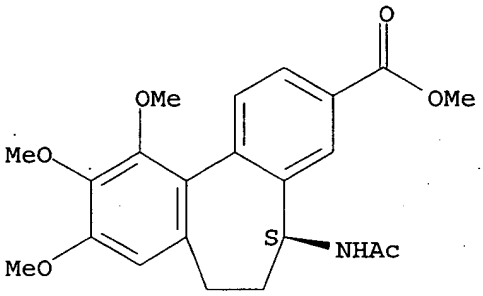
bis(trimethoxyphenyl)benzene II, and the tetramethoxydibenzocycloheptene III, were prepared and evaluated for their ability to prevent tubulin polymerization The bicyclic systems were prepared by coupling reaction of 2,3,4-trimethoxyphenylboronic acid with the appropriate bromoaryl ester. The x-ray structure of the most active compd III was determined

IT **641-28-1DP**, Allocolchicine, derivs. **146655-81-4P**
146655-83-6P 146655-84-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and tubulin-binding properties of)

RN 641-28-1 HCAPLUS

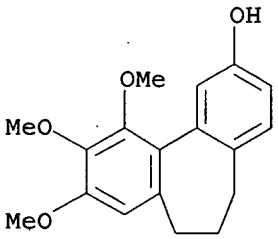
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



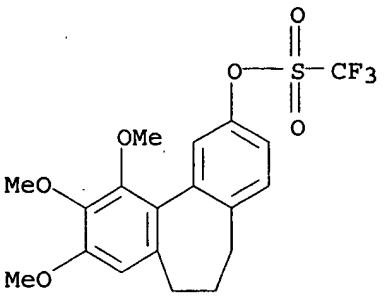
RN 146655-81-4 HCAPLUS

CN 5H-Dibenzo[a,c]cyclohepten-2-ol, 6,7-dihydro-9,10,11-trimethoxy- (9CI) (CA INDEX NAME)

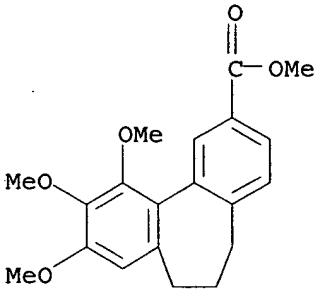


RN 146655-83-6 HCAPLUS

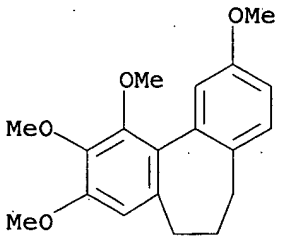
CN Methanesulfonic acid, trifluoro-, 6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-2-yl ester (9CI) (CA INDEX NAME)



RN 146655-84-7 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-2-carboxylic acid, 6,7-dihydro-9,10,11-trimethoxy-, methyl ester (9CI) (CA INDEX NAME)



IT **146655-82-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, crystal structure, and tubulin-binding properties of)
RN 146655-82-5 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene, 6,7-dihydro-1,2,3,10-tetramethoxy- (9CI) (CA INDEX NAME)



L24 ANSWER 30 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:511857 HCAPLUS
DOCUMENT NUMBER: 117:111857
TITLE: Fully regiocontrolled synthesis of deacetamidoisocolchicine: formal total synthesis of colchicine
AUTHOR(S): Banwell, Martin G.; Lambert, John N.; Corbett, Madeline; Greenwood, Richard J.; Gulbis, Jacqueline

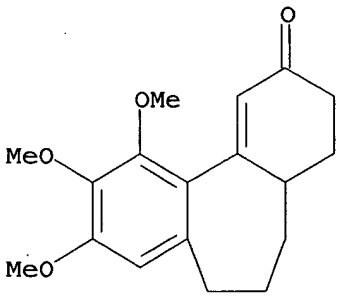
M.; Mackay, Maureen F.
CORPORATE SOURCE: Sch. Chem., Univ. Melbourne, Parkville, 3052, Australia
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (**1992**), (11), 1415-26
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:111857
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A 19-step synthesis of deacetamidoisocolchicine (I) was developed starting from com. available 3,4,5-trimethoxybenzaldehyde. Key elements of the strategy used include Robinson annulation of the benzosuberone II to produce the tricyclic enone III and elaboration of this latter compound to the tetracyclic α-methoxy enone IV. Base-promoted ring-expansion of IV then provided I, the acquisition of which constitutes a formal total synthesis of the alkaloid colchicine. In connection with efforts to optimize the yield of I, the novel acid-catalyzed conversion of V into dibenzocyclooctene VI has been observed The x-ray crystal structures of compound VI and a novel dichlorocarbene insertion product are reported.

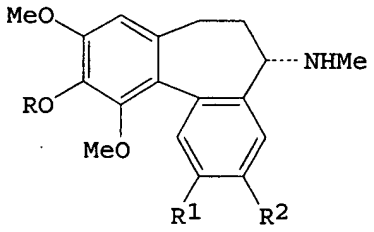
IT **131927-14-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acetoxylation of)

RN 131927-14-5 HCAPLUS
CN 2H-Dibenzo[a,c]cyclohepten-2-one, 3,4,4a,5,6,7-hexahydro-9,10,11-trimethoxy- (9CI) (CA INDEX NAME)



L24 ANSWER 35 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:55514 HCAPLUS
DOCUMENT NUMBER: 116:55514
TITLE: New natural dibenzocycloheptylamine alkaloids: a possible catabolic route for the colchicine alkaloids
AUTHOR(S): Abu Zarga, Musa H.; Sabri, Salim; Al-Tel, Taleb H.; Atta-ur-Rahman; Shah, Zahir; Feroz, M.
CORPORATE SOURCE: Chem. Dep., Univ. Jordan, Amman, Jordan
SOURCE: Journal of Natural Products (**1991**), 54(4), 936-40

CODEN: JNPRDF; ISSN: 0163-3864
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

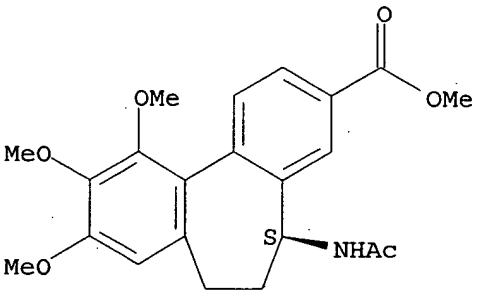
AB Colchicum decaisnei of Jordanian origin yielded 3 new alkaloids (-)-jerusalemine (I, R = H, R1 = OH, R2 = OMe), (-)-salimine (I, R = Me, R1 = CO2H, R2 = OMe), and (-)-suhailamine (I, R = Me, R1 = H, R2 = CO2Me), besides the known alkaloid (-)-androbiphenyline.

IT **641-28-1**, (-)-Suhailamine
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of Colchicum decaisnei, isolation and mol. structure of)

RN 641-28-1 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 40 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:529221 HCAPLUS
DOCUMENT NUMBER: 111:129221
TITLE: Spectroscopic and kinetic features of allocolchicine binding to tubulin
AUTHOR(S): Hastie, Susan Bane
CORPORATE SOURCE: Dep. Chem., State Univ. New York, Binghamton, NY, 13901, USA
SOURCE: Biochemistry (**1989**), 28(19), 7753-60
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Allocolchicine is a structural isomer of colchicine in which colchicine's tropone C ring is replaced with an aromatic ester. In spite of the structural differences between the 2 ligands, the association parameters for

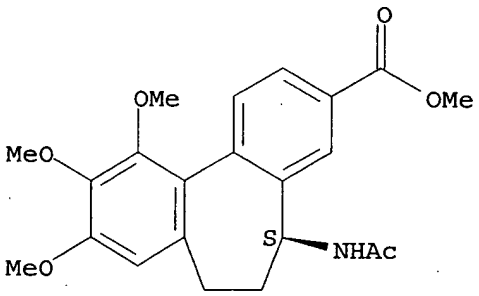
both mols. binding to tubulin are quite similar. The association constant for allocolchicine binding to tubulin was determined by fluorescence titration to be
6.1 + 105 M-1 at 37°, which is about a factor of 5 less than that of the colchicine-tubulin association In particular, anal. of the kinetics of the association of allocolchicine with tubulin yielded nearly equivalent activation parameters for the 2 ligands. The activation energy of the allocolchicine binding reaction was 18.4 kcal/mol, which is only slightly less than the activation energy for colchicine binding to tubulin. This finding argues against conformational flexibility of the C ring as the structural feature of colchicine responsible for the slow kinetics of colchicinoid-tubulin binding reactions. Tubulin binding promotes a dramatic enhancement of allocolchicine fluorescence. Unlike colchicine, the emission energy and intensity of the tubulin-bound allocolchicine fluorescence can be mimicked by solvent, and a general hydrophobic environment for the ligand binding site is indicated. The excitation spectrum of the protein-bound species, however, possesses 2 bands that center at higher and lower energy than the energy of the spectrum of the ligand in apolar solvents, indicating that properties of the colchicine binding site in addition to a low dielec. constant contribute to the fluorescence of the bound species. It is suggested that a π-stacking interaction between allocolchicine and an aromatic amino acid in the binding site may account for the unusual excitation spectrum of allocolchicine liganded to tubulin.

IT **641-28-1**, Allocolchicine
RL: BIOL (Biological study)
(tubulin binding by, kinetics and spectroscopic properties of, colchicine binding in relation to)

RN 641-28-1 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 45 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1983:72497 HCAPLUS

DOCUMENT NUMBER: 98:72497

TITLE: Circular dichroism. LXVII. Isolation and chemistry of the alkaloids from the plants of the subfamily Wurmbaeoideae. XCII. Circular dichroism of alkaloids of colchicine type and their derivatives

AUTHOR(S): Hrbek, Jaromir, Jr.; Hruban, Ladislav; Simanek, Vilim; Santavy, Frantisek; Snatzke, Gunther; Yemul, Srishalam S.

CORPORATE SOURCE: Med. Fac., Palacky Univ., Olomouc, 775 15, Czech.

SOURCE: Collection of Czechoslovak Chemical Communications (

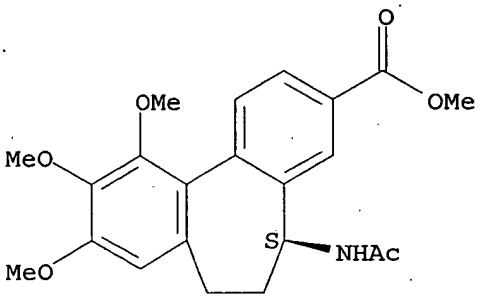
1982), 47(8), 2258-79
CODEN: CCCCAK; ISSN: 0366-547X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The CD spectra of 48 colchicine alkaloids and of some of their derivs. were given. The effects of the substituents and of the basic skeleton on the chiroptical properties of the measured compds. were discussed.

IT **641-28-1 6714-14-3**
RL: PRP (Properties)
(CD spectrum of)

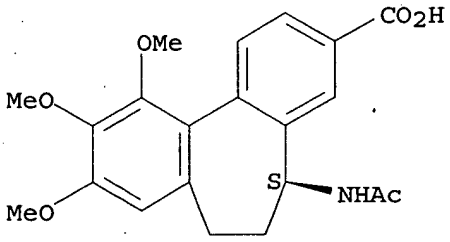
RN 641-28-1 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 6714-14-3 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 50 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1976:508833 HCAPLUS
DOCUMENT NUMBER: 85:108833
TITLE: Mass spectrometry of lumicolchicines and derivatives of allocolchicine
AUTHOR(S): Timbekov, E. Kh.; Kasimov, A. K.; Yusupov, M. K.; Aslanov, Kh. A.; Sadykov, A. S.
CORPORATE SOURCE: Tashk. Gos. Univ. im. Lenina, Tashkent, USSR
SOURCE: Izvestiya Akademii Nauk Turkmenskoi SSR, Seriya Fiziko-Tekhnicheskikh, Khimicheskikh i Geologicheskikh Nauk (**1976**), (1), 70-3
CODEN: ITUFAW; ISSN: 0002-3507
DOCUMENT TYPE: Journal

LANGUAGE: Russian

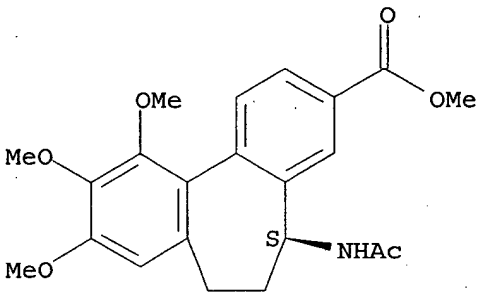
AB The mass spectral mol. ions of allocolchicine derivs. fragment via loss of AcNH2 and B ring decomposition with elimination of AcN:CH2. Lumicolchicine mol. ions undergo C and D ring decomposition with loss of CO and Me•. The mol. ions of the cis β-lumicolchicines are more intense than those of the γ-lumicolchicines.

IT **641-28-1 6714-14-3 42405-82-3**
42569-03-9
RL: PROC (Process)
(mass spectra fragmentation of)

RN 641-28-1 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

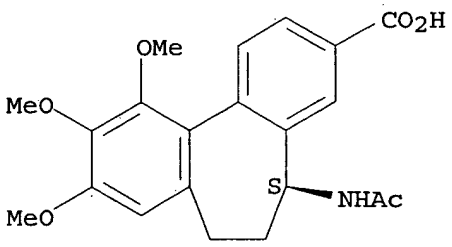
Absolute stereochemistry.



RN 6714-14-3 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, (5S)- (9CI) (CA INDEX NAME)

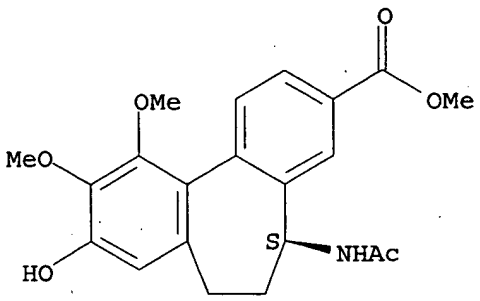
Absolute stereochemistry.



RN 42405-82-3 HCAPLUS

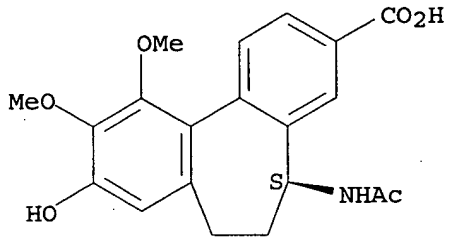
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9-hydroxy-10,11-dimethoxy-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



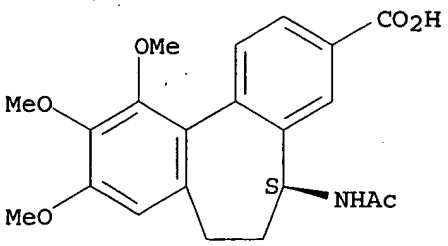
RN 42569-03-9 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9-hydroxy-10,11-dimethoxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



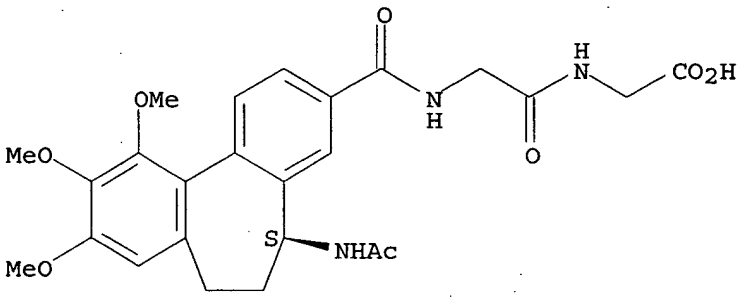
L24 ANSWER 55 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1971:420972 HCAPLUS
DOCUMENT NUMBER: 75:20972
TITLE: Aminocolchicine derivatives. VII
AUTHOR(S): Kiselev, V. V.
CORPORATE SOURCE: Inst. Eksptl. Klin. Onkol., Moscow, USSR
SOURCE: Zhurnal Obshchei Khimii (**1971**), 41(2), 464-6
CODEN: ZOKHA4; ISSN: 0044-460X
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Refluxing 11 hr glycylglycine with colchicine in MeOH with enough NaOH to maintain pH 10 gave 87% colchicidylglycylglycine monohydrate, [α]20D -195.5°. Similarly was prepared colchicidylglycyl-D-valine. Colchicidyl-L-lysine heated with 10% HCl 2 hr and the product treated with hot EtOH gave deacetylcolchicidyl-L-lysine. The Cu complex from L-ornithine-HCl and colchicine in aqueous MeOH was heated 5 hr until green and after concentration and addition of H2S gave amorphous colchicidyl-L-ornithine. Heating colchicidyl-D-valine with 18% HCl gave deacetylglycylglycine, valine and glycine.
IT **6714-14-3DP**, Colchicic acid, peptide derivs. **32790-58-2P** **32790-59-3P** **32790-60-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 6714-14-3 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

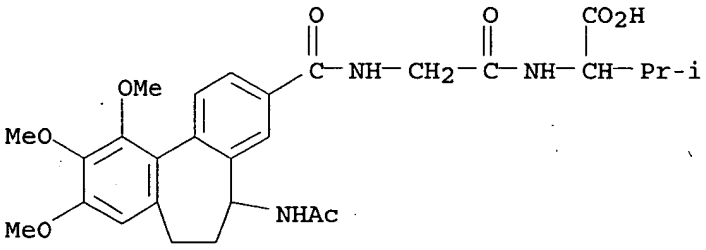


RN 32790-58-2 HCAPLUS
CN Glycine, N-[N-[(5-acetamido-6,7-dihydro-9,10,11-trimethoxy-5-H-dibenzo[a,c]cyclohepten-3-yl)carbonyl]glycyl]-, (S)- (8CI) (CA INDEX NAME)

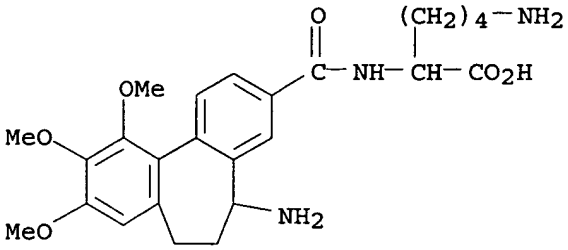
Absolute stereochemistry.



RN 32790-59-3 HCAPLUS
CN Valine, N-[N-[(5-acetamido-6,7-dihydro-9,10,11-trimethoxy-5-H-dibenzo[a,c]cyclohepten-3-yl)carbonyl]glycyl]-, (5S)-D- (8CI) (CA INDEX NAME)



RN 32790-60-6 HCAPLUS
CN Lysine, N2-[(5-amino-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-3-yl)carbonyl]-, (5S)-L- (8CI) (CA INDEX NAME)



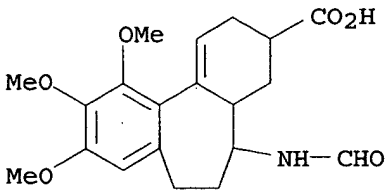
L24 ANSWER 60 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1963:40191 HCAPLUS
DOCUMENT NUMBER: 58:40191
ORIGINAL REFERENCE NO.: 58:6876b-h,6877a-h,6878a-b
TITLE: Total synthesis of dl-colchiceine. I. Synthesis of 3-hydroxy-9,10,11-trimethoxy-1,2,3,4,6,7-hexahydro-5H-dibenzo-[a,c]cycloheptatrien-5-one
AUTHOR(S): Nakamura, Takahiro; Murase, Yasuhiro; Hayashi, Ryozo; Endo, Yonekichi
CORPORATE SOURCE: Sankyo Co., Tokyo
SOURCE: Chemical & Pharmaceutical Bulletin (**1962**), 10, 281-90
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. CA 55, 18791f. Catalytic hydrogenation (Raney Ni) of 200 cc. OC(CH2CH2CO2Et)2 in MeOH yielded 200 g. HOCH(CH2CH2CO2Et)2 (I), which was distilled to give the γ-lactone (II), b0.005 134.5°. Therefore, I was subjected without distillation to the Dieckmann cyclization with NaH in dry Et2O-C6H6 to yield 57% Et 2-oxo-5-hydroxycyclohexanecarboxylate (III), b0.1. 123°; 2,4-dinitrophenylhydrazone m. 164°. The Pechmann condensation of III and pyrogallol with POCl3 in dry C6H6 yielded 60% 3,4,8-(HO)3 derivative (IV) (R = R' = H) of V, m. 288°. The coumarin (rather than chromone) structure of IV was confirmed by ring cleavage with KOH in the presence of Me2SO4 to give the coumaric acid, VI (R = H), m. 159°. The Pechmann condensation of III was unsuccessful with 3,4,5-MeO(HO)2C6H2CH2CH2CO2H(VII), m. 95°, which had been obtained in 80% yield by the catalytic hydrogenation (PdCl2) of 3,4,5-MeO(HO)2C6H2CH:CHCO2H (VIII), m. 182°, obtained in turn in 51% yield from 3,4,5-MeO(HO)2C6H2CHO with CH2(CO2H)2 in C5H5N in the presence of PhNH2. Therefore III was condensed with 2,3-(HO)2C6H3OMe in the presence of MeHSO3 (in place of POCl3) to give a quant. yield of V (R = Me, R' = H) (IX), m. 261°, which, like IV, also gave VI on ring cleavage with KOH. IX boiled 16 hrs. with CH2:CHCH2Br and K2CO3 in dilute MeOH yielded 66% 4-CH2:CHCH2O derivative of IX, m. 112°, which was rearranged by heating 6 hrs. with PhNMe2 under N to yield 87% V (R =Me,R' = CH2CH:CH2) (X), m. 182°, and this was isomerized by heating with KOH-MeOH to yield 73.5% V (R = Me, R' = MeCH:CH) (XI), m. 229°. Ozonization of XI in the cold with only 1 mole O3 (more than 1 mole cleaved the coumarin ring) yielded 67.7% V (R = Me, R' = CHO) (XII), m. 253°. The coumarin structure of XII was confirmed by treatment with alkali and Me2SO4 (as IV was treated) to yield 60% VI (R = CHO) (XIII), m. 156°. XII underwent the Knoevenagel condensation by heating 22 hrs. at 50° with CH2(CO2H)2 in C5H5N containing PhNH2 to yield 87.6% V [R = Me, R' = CH:C(CO2H)2] (XIV), m. 260° (decomposition), which was catalytically hydrogenated (Pd-C) in MeOH to yield 90% V [R =

Me, R' = CH2CH(CO2H)2] (XV), m. 248°, and this (1 g.) was decarboxylated by heating 20 hrs. in vacuo at 140-50° to yield 0.85 g. V (R = Me, R' = CH2CH2CO2H) (XVI), m. 245°. Cleavage of the coumarin ring of XV with alkali and Me2SO4, as for IV, yielded 46.7% VI [R = CH2CH(CO2H)2] (XVII), m. 183° (decomposition), and this (0.46 g.) was decarboxylated, as was XV, by heating only 2 hrs. (in place of 20 hrs.) to yield 0.41 g. VI (R = CH2CH2CO2H) (XVIII), m. 184°, formed also in 53% yield by cleavage of the coumarin ring of XVI with alkali and Me2SO4. Treatment of XVIII either with MeOH and concentrated H2SO4 or with CH2N2 esterified both CO2H groups to yield 93 and 100%, resp., diester (XIX), b0.001 240° (bath temperature), and this underwent the Dieckmann condensation with tert-BuOK in xylene under N to give the crude cyclized β-oxocarboxylate, which was saponified and decarboxylated to yield 4.5% title compound (XX), m. 84°; 2,4-dinitrophenylhydrazone m. 101°. XX (30 mg.) was also formed by cyclization of 0.3 g. XVIII by boiling 2 hrs. under N with Ac2O and AcOK. The presence of a double bond conjugated with the Ph ring in XX was supported by heating 1 g. XX under N with NH2CHO and HCO2H to yield 147 mg. XXI, m. 161°. The ultraviolet and infrared absorption spectra of both XX and XXI confirmed the conjugation of the double bond with the Ph ring. Since the CO group in the B-ring of XX would interfere with extension of the C-ring to a 7-membered ring (as in colchicine) attempts were made to form a 7-membered ring ketone first, followed by cyclization of tile B-ring. Therefore, XIX and the Me ester (XXII) of XVII, b0.001 190° (bath temperature), were separately oxidized with CrO3-C5H5N to yield, resp., 49.3 and 39% corresponding 5-oxo compds. (XXIII and XXIV), both of which gave large amts. of reddish orange precipitate with 2,4-dimtrophenylhydrazine. However, all attempts for ring enlargement of the C-ring of XXIII and XXIV failed. Infrared data were reported and discussed in support of the structures of I-IV, VI-XXII, and XXIV, and ultraviolet data for VI-IX, XIV, XV, XVII, XVIII, XX, XXI, and XXIII.

IT **100212-69-9**, 2H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-formamido-3,4,4a,5,6,7-hexahydro-9,10,11-trimethoxy-
(preparation of)

RN 100212-69-9 HCAPLUS

CN 2H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-formamido-3,4,4a,5,6,7-hexahydro-9,10,11-trimethoxy- (7CI) (CA INDEX NAME)



L24 ANSWER 65 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1961:13550 HCAPLUS

DOCUMENT NUMBER: 55:13550

ORIGINAL REFERENCE NO.: 55:2708a-d

TITLE: Thiocolchicine. VI. Lactams obtained by contraction of the tropone ring

AUTHOR(S): Muller, Georges; Vaterlaus, Bruno P.; Velluz, Leon

SOURCE: Bulletin de la Societe Chimique de France (**1957**), 5, 434-5
CODEN: BSCFAS; ISSN: 0037-8968

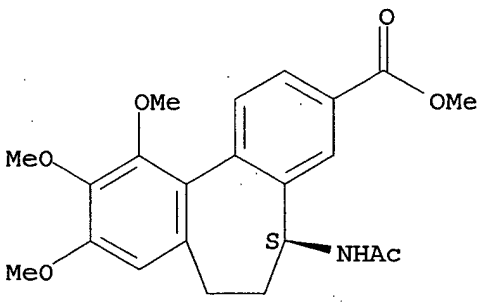
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Thiocolchicine (I) gave with MeSNa (II) a mixture of 1,2,3-trimethoxy-7-acetylaminodibenzo[a,c]cycloheptane-9-carboxylic acid (III) and 1,2,3-trimethoxy-7-amino-9-methylthio-7a,8-dihydrodibenzo[a,c]cycloheptane-8-carboxylic acid 7,8-lactam (IV). The structure of IV followed from its spectrum and from its conversion to fully aromatic derivs. I (10 g.), 5.3 g. II, and 60 ml. MeOH was kept 3 days at room temperature, 200 ml. CHCl3 added, the mixture washed, dried, evaporated to dryness, the residue taken up in CHCl3, and chromatographed on Al2O3. Elution with CHCl3 gave successively 3 g. III Me ester, m. 250°, and 2.7 g. I, and with 1% EtOH in CHCl3 gave 2.1 g. IV, yellow crystals, m. 258° (EtOAc then EtOH), [α]D -380 ± 20° (c 0.5 CHCl3), λ 374 mμ (ε 15,900), ν 1686 cm.-1 (γ-lactam). IV (250 mg.), 5 cc. 10N aqueous NaOH, and 45 cc. EtOH was kept 2 days at room temperature, the mixture neutralized, extracted with CHCl3, the extract washed, dried, and evaporated to dryness, and the residue recrystd. from EtOH to give 145 mg. 1,2,3-trimethoxy-7-amino-9-methylthiodibenzo[a,c]cycloheptane-8-carboxylic acid 7,8-lactam (V), m. 252°, [α]D 80 ± 5° (c) 0.5, CHCl3), λ 289 mμ (ε 23,650), ν 1690 cm.-1 V (83 mg.), 0.5 cc. EtOH suspension of 1% Pd-Raney Ni, and 100 cc. EtOH was refluxed 5 hrs., the solution filtered, the filtrate evaporated to dryness and the residue recrystd. from C6H6-ligroine to give 57 mg. 1,2,3-trimethoxy-7-aminodibenzo[a,c]cycloheptane-8-carboxylic acid 7,8-lactam (VI), m. 193-4°, [α]D 150 ± 5° (c 0.5, EtOH), ν 1690 cm.-1 The antimitotic activity of IV and V was similar to that of deacetyl derivative of I; VI was inactive.

IT **641-28-1**, Colchicic acid, methyl ester **6714-14-3**, Colchicic acid
(preparation of)

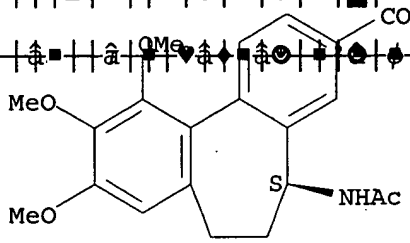
RN 641-28-1 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 6714-14-3 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



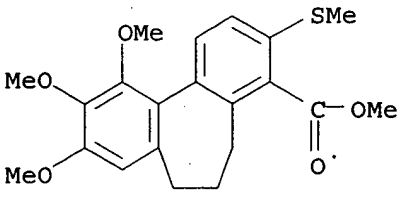
L24 ANSWER 70 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1958:82512 HCAPLUS
DOCUMENT NUMBER: 52:82512
ORIGINAL REFERENCE NO.: 52:14578d-e
TITLE: Degradation of a quaternary thiocolchicine with the elimination of nitrogen
AUTHOR(S): Vaterlaus, Bruno P.; Furlenmeier, Andre E.
SOURCE: Bulletin de la Societe Chimique de France (**1957**) 1481-3
CODEN: BSCFAS; ISSN: 0037-8968
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 52:82512

AB Deacetylated I (VII) in MeOH treated at room temperature with MeI in the presence of Na2CO3 gave the N-Me derivative which was converted in pyridine-Ac2O to the N,N-di-Me derivative, m. 169-70° (decomposition)(AcOEt), [α]20D -150 ±5° (0.5%, CHCl3); methiodide, m. 201-3° (decomposition). The methiodide in 92% MeOH (by volume) treated with freshly prepared Ag2O and heated at 40° after the evolution of NMe3 gave VIII, m. 159-60° (MeOH), [α]20D 0° (0.5%, CHCl3). VIII (AcOEt solution) hydrogenated in the presence of Raney Ni previously washed in H2O and EtOH eliminated its SMe group, resulting in the carbomethoxy derivative, m. 152°, [α]20D 0°. Saponification of this compound with NaOH in MeOH gave the free acid, m. 184° (Et2O).

IT **115003-37-7**, 5H-Dibenzo[a,c]cycloheptene-4-carboxylic acid, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, methyl ester
(preparation of)

RN 115003-37-7 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-4-carboxylic acid, 6,7-dihydro-9,10,11-trimethoxy-3-(methylthio)-, methyl ester (6CI) (CA INDEX NAME)



L24 ANSWER 75 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1956:66028 HCAPLUS
DOCUMENT NUMBER: 50:66028
ORIGINAL REFERENCE NO.: 50:12304e-f

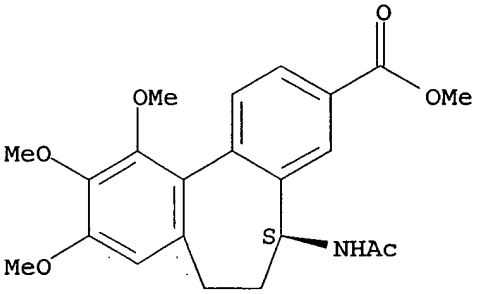
TITLE: Comparison of the effect of thyroxine on basal metabolism and on oxidative phosphorylation
AUTHOR(S): Martius, Carl; Bieling, Hans; Nitz-Litzow, Dagobert
CORPORATE SOURCE: Univ. Wurzburg, Germany
SOURCE: Biochemische Zeitschrift (**1955**), 327, 163-9
CODEN: BIZEA2; ISSN: 0366-0753
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The decrease in phosphorylation rate in the diaphragm and liver mitochondria of guinea pigs and rats has a definite relation to the increase in basal metabolism, and each can be calculated from the other. Thyroxine has a greater influence on the 1st step of oxidative phosphorylation than on the 2 following ones.

IT **641-28-1**, Colchicic acid, methyl ester **116104-34-8**, Colchicic acid, N-methyl- **116534-08-8**, Colchicic acid, N-methyl-, methyl ester
(pharmacol. of)

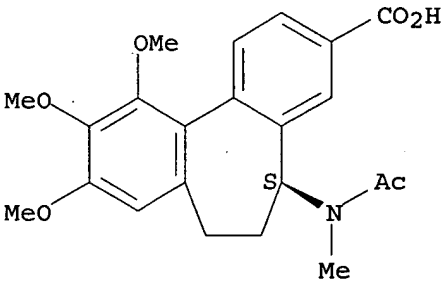
RN 641-28-1 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



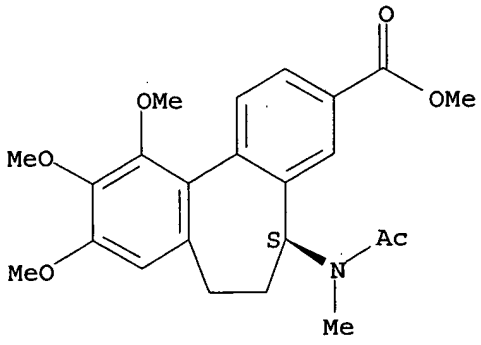
RN 116104-34-8 HCAPLUS
CN Colchicic acid, N-methyl- (6CI) (CA INDEX NAME)

Absolute stereochemistry.



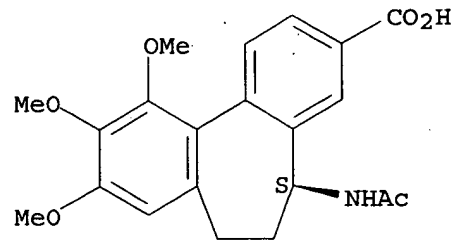
RN 116534-08-8 HCAPLUS
CN Colchicic acid, N-methyl-, methyl ester (6CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 80 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1953:63170 HCAPLUS
DOCUMENT NUMBER: 47:63170
ORIGINAL REFERENCE NO.: 47:10734e-f
TITLE: Damage induced in sarcoma 37 with chemical agents. V. Derivatives of colchicine and isocolchicine
AUTHOR(S): Leiter, J.; Hartwell, J. L.; Ullyot, G. E.; Shear, M. J.
CORPORATE SOURCE: Natl. Cancer Inst., Bethesda, MD
SOURCE: Journal of the National Cancer Institute (1940-1978) (**1953**), 13, 1201-11
CODEN: JNCIAM; ISSN: 0027-8874
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 47, 2889h. The iso-forms of 4 potent colchicine derivs. (colchicine, its Et ether, colchiceinamide, and trimethylcolchicinic acid Me ether d-tartrate) were inactive toward sarcoma 37. Colchiceine Et ether and demethylcolchicine damaged sarcoma 37; hexahydrocolchicine was less effective; and hexahydrocolchiceine, colchinoic acid, its Me ester, and N-benzoylcolchinic anhydride were inactive. The relation between chemical structure and potency is discussed.
IT **6714-14-3**, Colchinoic acid
(as name for colchicic acid)
RN 6714-14-3 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, (5S)- (9CI) (CA INDEX NAME)

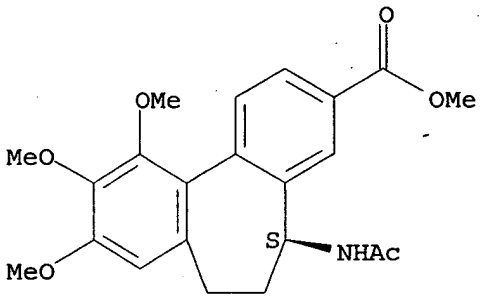
Absolute stereochemistry.



IT **641-28-1**, Colchicic acid, methyl ester
(sarcoma damage by)
RN 641-28-1 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-

9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



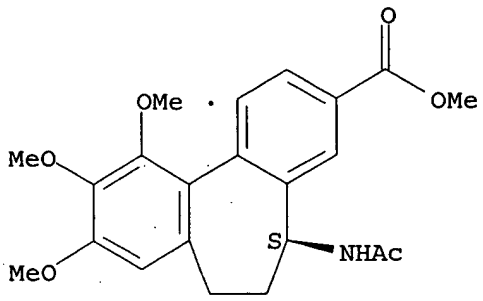
L24 ANSWER 85 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1951:12206 HCAPLUS
DOCUMENT NUMBER: 45:12206
ORIGINAL REFERENCE NO.: 45:2152b-d
TITLE: Isolation of new compounds from Colchicum autumnale. XII. Compounds of Colchicum autumnale and their derivatives
AUTHOR(S): Santavy, F.; Reichstein, T.
CORPORATE SOURCE: Univ., Basel, Switz.
SOURCE: Helvetica Chimica Acta (**1950**), 33, 1606-27
CODEN: HCACAV; ISSN: 0018-019X
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C.A. 44, 9518i(in German). Extraction of the plant seeds and chromatography on Al2O3 resulted in the isolation of 4 crystalline substances in addition to colchicine (A). Compound B, C21H23O6N, decompose 264-7°, [α]22D -171.2° (CHCl3), was identical with N-formyldesacetylcolchicine. Compound C, C21H23O6N, m. 176-82°, [α]22D -130.7° (CHCl3), was converted with CH2N2 to A from which it differs only by substitution of one OH for one MeO. C and MeCHN2 gave the corresponding Et ether, m. 232-4°, [α]23D -135.8° (CHCl3). Ac derivative of C, m. 231-3°, [α]20D -115° (in CHCl3), gave on boiling with NaOMe desmethylcolchicinic acid C (I), m. 258-60°, which gave the known colchicinic acid Me ester with CH2N2. Acetylation and methylation of I gave acetyldesmethylcolchicinic acid Me ester, C23H25O7N, m. 234-6°. Compound G, C22H25O6N or C23H27O6N, m. 187-9°, [α]19D -139.2° (CHCl3), gave colchiceine on heating with dilute HCl and colchicinic acid with NaOMe and is either a homolog or isomer of A. Colchiceine and MeCHN2 gave isoethylcolchiceine, C23H27O6N, m. 215-18°/223-5°, [α]19D -293.7° (CHCl3) and not identical with G. Compound J, m. 184-6°, [α]23D 307.6° (CHCl3) is probably an isomer of A. Several other newly isolated compds. are briefly described.

IT **641-28-1**, Colchicic acid, methyl ester **6714-14-3**, Colchicic acid
(preparation of)

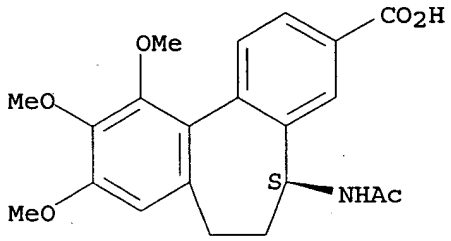
RN 641-28-1 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 6714-14-3 HCAPLUS
CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 87 OF 87 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1948:27498 HCAPLUS
DOCUMENT NUMBER: 42:27498
ORIGINAL REFERENCE NO.: 42:5891a-d
TITLE: Preparation of colchicic acid from colchicine
AUTHOR(S): Santavy, Fr.
CORPORATE SOURCE: Univ. Basel, Switz.
SOURCE: Helvetica Chimica Acta (**1948**), 31, 821-6
CODEN: HCACAV; ISSN: 0018-019X
DOCUMENT TYPE: Journal
LANGUAGE: French

AB In an attempt to prepare N-methylcolchicine from colchicine (I), 1 g. I is heated in a sealed tube with 0.8 g. MeI and 5 cc. MeOH containing 0.1 g. Na at 100°, the MeOH distilled off in vacuo at 30°, and the residue acidified with 2 N HCl, giving crude colchicic acid (II), m. 240-60°. I (100 mg.) is refluxed in 2 cc. MeOH, 5 cc. MeOH containing 0.1 g. Na added, the mixture heated slowly to boiling, kept there 0.5 hr., the MeOH distilled off in vacuo at 30°, and the residue taken up in 5 cc. H2O and slightly acidified with HCl, giving 70-80% crude or 50-60% pure II, m. 262-6°. When 100 mg. I in 2 cc. MeOH and 0.2 cc. H2O is heated with 5 cc. MeOH containing 0.1 g. Na, 45% II is formed. I heated with a saturated MeOH-KOH solution gives 25-35% II. Iso-colchicine heated with MeONa in MeOH also gives II. Colchiceine treated in the same way is recovered unchanged. II, fine needles from CHCl3, EtOAc, or Me2CO-ether, m. 262-6° and sublimes at 240°/0.001 mm. Methylation of 500 mg. II with an excess of CH2N2 in MeOH, evaporation of the MeOH, and extraction of the residue with MeOH or CHCl3 leaves a residue, m. 131-3°. From

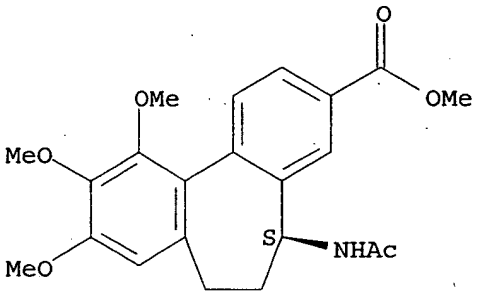
the extract Me colchicate (III), prisms, m. 261-2°, [α]20D -141.72 ± 2° (c 1.4112, CHCl3), subliming 220°/0.001 mm., is isolated. III treated with Ac2O in C5H5N is recovered unchanged. Saponification of III with MeOH-NaOH gives II, λmaximum 280 mμ, λmin. 257 mμ (in 0.05 N NaOH). The polarographic curve of II is given.

IT **641-28-1**, Colchicic acid, methyl ester **6714-14-3**, Colchicic acid
(preparation of)

RN 641-28-1 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, methyl ester, (5S)- (9CI) (CA INDEX NAME)

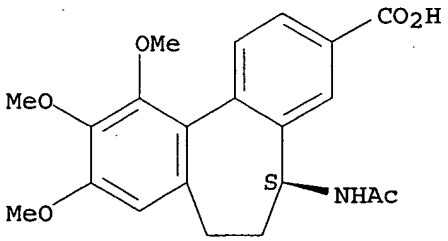
Absolute stereochemistry.



RN 6714-14-3 HCAPLUS

CN 5H-Dibenzo[a,c]cycloheptene-3-carboxylic acid, 5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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